CYTOKERATIN PATTERNS OF THE EPITHELIAL AND NON-EPITHELIAL PROLIFERATIVE LESIONS OF THE RAT RESPIRATORY TRACT

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The differential expression of cytokeratin (CK) polypeptides is a well established tool in the differential diagnosis of human lung cancer. The objective of this study was to investigate whether there are differences in the CK expression patterns between different types of proliferative lesions in the rat respiratory tract. Serial sections (formalin-fixed and paraffin-embedded) of the proliferative lesions (3 in the nose of rats exposed to inhaled irritants, 21 in the lungs of unexposed control rats including metastases of other epithelial and non-epithelial primary proliferative lesions) were immunohistochemically stained employing an antibody panel characterized for the rat analogues of CK8, CK18, CK7, CK19, CK14, CK15, CK4, CK13, and CK1,10/11 [Schlage et al., Toxicol. Pathol. 26, 324-343 (1998)]. These lesions were evaluated for the staining patterns using a 4-stage individual grading for intensity as well as for distribution. In the nose, the adenoma had intense staining for CK14, CK15 (patchy to diffuse) and for CK18, CK19 (focal to patchy), while the nasal squamous cell carcinomas had additional staining for CK8, CK4, CK13, and CK1,10/11 (focal to patchy). In the lung, alveolar hyperplasia had intense staining only for CK7, CK8, CK18, and CK19 and in 1 of 4 cases for CK 4. In addition to this CK pattern, bronchiolo-alveolar adenomas had focal staining for CK4 (4 of 6) and bronchiolo-alveolar carcinomas for CK4 (3 of 3), for CK13 and CK15 (1 of 3), and for CK14 and CK1,10/11 (2 of 3), thereby resembling the basic CK patterns of human lung tumors. In conclusion, the differences in CK patterns seen for different epithelial proliferative lesions may prove to be a valuable diagnostic tool. However, the number of lesions examined was not large enough to make a conclusive statement with regard to differential cytokeratin patterns for proliferative lesions in the rat respiratory tract. Currently, we are evaluating a larger number of lesions from a 30-month inhalation study with room-aged cigarette sidestream smoke and diesel engine exhaust in order to validate the CK expression analysis in the rat lung.

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